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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PENG, BO	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,354	VAN DER WERF ET AL.	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *21-27,30 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,28,29 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/11/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *attachment*.

DETAILED ACTION

1. This Office action is in response to the amendment filed on October 22, 2010. New Claim 32 has been added. Claims 1-32 are pending. Claims 21-27, 30 and 31 have been withdrawn. Claims 1-4, 28, 29 and 32 are examined in this Office action. Since new rejection is made in this Office action, the Office action is made non-final.

Claim Objection

2. (**Prior objection-maintained**) The objection to Claim 28 for containing a non-elected invention of "an antibody claimed in Claim 21" is maintained. Correction is required.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. (**Prior rejection-withdrawn**) The rejection of Claims 1, 28 and 29 under 35 U.S.C. 102(a) as being anticipated by Marra, et al. (Science 300 (5624), 1399-1404 (2003, cited in IDS), as evidenced by Genbank AY274119.3 GI:30248028, **is withdrawn** in view of applicants' argument.

5. (**New rejection**) Claims 1, 28, 29 and 32 are rejected under 35 U.S.C. 102(a) as being anticipated by Rota et al. (Science 300 (5624), 1394-9. Epub 2003 May 1, cited in IDS), as

evidenced by Genbank AY278741 (attached to this Office action).

6. Rota et al teach an isolated and purified S protein of SARS-CoV Urbani strain (see e.g. Fig. S4), which has an amino acid sequence 100% identical to the claimed S protein having the sequence of SEQ ID NO: 3; see attached sequence alignment. Rota teaches that the whole sequence of SARS-CoV Urbani strain is shown by Genbank AY278741 (see e.g. Para 3, right col. p. 1394). Genbank AY278741 is attachment to this Office action. Thus, the claimed subject matter of Claims 1, 28, 29 and 32 is anticipated by Rota.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. (**Prior rejection-maintained**) The rejection of Claims 2, 28 and 29 under 35 U.S.C. 103(a) as being unpatentable over Vilalta et al (US 20070105193, Provisional application 60/482505, filing date June 26, 2003), **is maintained** for the reason of record.

In response to applicants' argument:

9. The applicants argue that the applicants had deposited a cDNA encoding the complete S protein by June 20, 2003--which is earlier than the June 26, 2003 priority date of Vilalta asserted by the Office. Accordingly, Vilalta is not prior art to this application. The rejection is therefore should be withdrawn.

10. Applicants' argument is considered but not found persuasive. Applicants' deposit of a cDNA encoding the complete S protein on June 20, 2003, is noted. However, Claims 2, 28 and 29 are not directed to a cDNA encoding the complete S protein, rather, they are drawn to an S protein fragment **consisting of** the amino acids corresponding to the amino acids 1 to 1193 of SEQ ID NO: 3. Applicants have not provided explicit description for the claimed S fragment **consisting of** 1-1193 until December 2, 2003, the filing date of France 0314151. Thus, Vilalta is proper prior art for Claims 2, 28 and 29. The rejection is therefore maintained.

11. (**Prior rejection-withdrawn**) The rejection of Claims 1-4, 28 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marra, et al. (Science 300 (5624), 1399-1404 (2003), in view of Genbank AY274119.3 GI:30248028, **is withdrawn** in view of applicants' argument. A new rejection is set forth below:

12. (**New rejection**) Claims 1-4, 28, 29 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rota et al. (Science 300 (5624), 1394-9. Epub 2003 May 1), Marra, et al. (Science 300 (5624), 1399-1404 (2003) and Wang (Clinical Chemistry, 49(12):1989-1996; Published on Nov. 13, 2003; cited in IDS).

13. Claims 1-4, 28 and 29 are directed to a polypeptide having the ectodomain or a fragment of the ectodomain of S protein of SEQ ID NO: 3, wherein the polypeptide consists of the amino acids 1-1193, 14-1193, and 475-1193 of S protein.

14. The relevance of Rota is set forth supra. In addition, Rota teaches that S proteins contain important virus-neutralizing epitopes; and amino acid changes can dramatically affect the virulence and in vitro host cell tropisim of the virus; see lines 4-8, middle col. p. 1397.

Moreover, amino acid 1191-1255 of S protein is membrane domain and cytoplasmic tail; see Para 1, middle col. and Fig. 3; p.1397. These teachings indicate to one of ordinary skill in the art that the S fragment 1-1191 is soluble (not membrane bound) and contains biological important properties.

15. However, Rota et al. do not explicitly teach an S polypeptide **consisting of** amino acids 1-1193, 14-1193, or 475-1193 of the S protein of SEQ ID NO: 3 (Claims 2-4).

16. Marra et al. teaches that SARS S protein Tor2 strain, which is substantially same as S protein of SEQ ID NO:3 (Urbani strain), except one amino acid; see Table 1. Marra et al. teach that S protein is a type I membrane protein with a signal peptide of amino acids 1-13, which has cleavage site at residues 13, see Para 1, left col. p. 1402. Marra teaches: "The majority of the protein (**residues 14 to 1195**) on the outside of the cell surface or virus particle, in agreement with other coronavirus Spike protein data"; see the bridging sentence between the left col. and the middle col., p. 1402. Marra et al indicate that SARS proteins and genome are useful for development of immunological tests, for the development of neutralizing antibodies, and for the identification of putative epitopes for vaccine development, see e.g. Abstract, and the Para bridging middle and right col., p. 1403.

17. Wang teaches that S fragments from amino acids 582-906 of S protein can react with sera from SARS patients; see e.g. Table 1. Amino acids 585-645 is most antigenic reactive to sera from SAR patients; see e.g. Fig. 1, up panel. An epitope is located around amino acid 599 of S protein; see e.g. Abstract.

18. It would have been obvious to one of ordinary skill in the art at the time the invention was made to make S fragments containing ectodomain, such as amino acids 1 -1193, 14-1193, or

475-1193 of the S protein of SEQ ID NO: 3 (Claims 2-4) for following reasons: The Supreme Court provided a number of bases on which a claimed invention may be found obvious. In particular, "When there is a design need or market pressure to solve a problem and there are a finite number of identified predictable potential solutions, a person of ordinary skill has good reason to pursue the known potential options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense" (KSR International Co. v. Teleflex Inc. (82 U.S.P.Q. 2d1385, 2007). In the present case, the prior art has provided that there is a design need or market pressure to make antigens (immunogens) for immunological tests for detecting SARS virus, for developing neutralizing antibodies to SARS virus, and identifying epitopes for vaccine development, see e.g. Marra et al. Abstract, and the Para bridging middle and right col., p. 1403. The prior art has also provided a finite number of identified predictable potential solutions for making the instant S fragments of the ectodomain of S protein: (1) The prior art reference has disclosed S protein, which is identical to the instant SEQ ID NO: 3, as taught by Rota; (2) Both Rota and Marra et al. has provided structural characterization of S protein. Specifically, S protein is a type I membrane protein, wherein amino acids 1-1191, and 14-1195, are on the outside of the cell surface or virus particle, and are not membrane bound. (3) Wang teaches that amino acids 585-645 of S protein is most antigenic to sera from SAR patients; see e.g. Fig. 1, up panel. An epitope is located around amino acid 599 of S protein; see e.g. Abstract. In view of these teachings, one of ordinary skill in the art would motivated to make S fragments containing the ectodomain of S protein, such as a.a.1 -1193, a.a. 14-1193, or a.a. 475-1193, or their equivalents, because soluble viral fragments (not membrane-bound) that exposed on the surface of viral particles are known to be good

antigens (immunogens) for vaccine component, or antigens for immunological assays (e.g. ELISA, antibody assays). There would have been a reasonable expectation of success in making such S fragments by routing molecular cloning technique, given that the sequence of S protein is readily available; as taught by Rota. In turn, because the claimed S polypeptides have the properties taught by the prior art, it would have been obvious to make the claimed S fragments. Therefore, the claimed invention is obvious over Rota, Marra and Wnag, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. (**New rejection**) Claims 1-4, 28, 29 and 32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 22-28, 30-31, 35-48 of copending Application No. 12/665,090 ('090). Although the conflicting claims are not

identical, they are not patentably distinct from each other because Claims 1-4, 28, 29 and 32 of the instant application is obvious variation of the invention defined in the co-pending application '090, in view of Einhauer (J. Biochem. Biophys. Methods 49(2001)455-465), Vilalta et al (US 20070105193) and Moore A. et al.(Vaccine 17 (1999) 2517-2527).

20. Claims 22-28, 30-31, and 35-48 of copending Application '090 are directed to an immunogenic composition comprising:(a) an immunogenic SARS coronavirus S (spike) polypeptide; and (b) an adjuvant comprising a lipopolysaccharide, a saponin and a liposome; wherein the S polypeptide comprises the extracellular domain of the S protein; wherein the S polypeptide comprises amino acids 14 to 1193 of the SARS-CoV S protein fused at the C-terminal to the sequence SGDYKDDDDK.

21. Einhauer teaches that SGDYKDDDDK, known as FLAG peptide, which includes an enterokinase-cleavage site. FLAG fused protein is specifically designed for isolate the protein by immunoaffinity chromatography; see e.g. Abstract. FLAG sequence can be removed to recover the peptide of interst.

22. Vilalta et al (US 20070105193) teaches that adjuvants and liposome can added to an antigen to enhance immune responses; see Para [0258][0275].

23. Moore teaches the adjuvant combination monophosphoryl lipid A and QS21 can switches T cell responses induced with a soluble recombinant protein antigen from Th2 to Th1

24. It would have been obvious to one of ordinary skill in the art at the time the invention was made to make S peptides of the instant claims in order to use them in the immunogenic composition, and to use them in the method of eliciting immune response to SARS of co-pending

application '090. Thus, the invention of the instant claims was clearly prima facie obvious over the invention defined in the co-pending application '090.

25. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Remarks

26. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on Tu-F, 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/
Primary Examiner, Art Unit 1648